Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents

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HIV and the Older Patient (Last updated March 27, 2012; last reviewed March 27, 2012)

Key Considerations When Caring for Older HIV-Infected Patients
• Antiretroviral therapy (ART) is recommended in patients >50 years of age, regardless of CD4 cell count **(BIII)**, because the risk of non-AIDS related complications may increase and the immunologic response to ART may be reduced in older HIV-infected patients.
• ART-associated adverse events may occur more frequently in older HIV-infected adults than in younger HIV-infected individuals. Therefore, the bone, kidney, metabolic, cardiovascular, and liver health of older HIV-infected adults should be monitored closely.
• The increased risk of drug-drug interactions between antiretroviral (ARV) drugs and other medications commonly used in older HIV-infected patients should be assessed regularly, especially when starting or switching ART and concomitant medications.
• HIV experts and primary care providers should work together to optimize the medical care of older HIV-infected patients with complex comorbidities.
• Counseling to prevent secondary transmission of HIV remains an important aspect of the care of the older HIV-infected patient.
Rating of Recommendations: *A = Strong; B = Moderate; C = Optional*
Rating of Evidence: *I = data from randomized controlled trials; II = data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = expert opinion*

Effective antiretroviral therapy (ART) has increased survival in HIV-infected individuals, resulting in an increasing number of older individuals living with HIV infection. In the United States, approximately 30% of people currently living with HIV/AIDS are age 50 years or older and trends suggest that the proportion of older persons living with HIV/AIDS will increase steadily.[1] Care of HIV-infected patients increasingly will involve adults 60 to 80 years of age, a population for which data from clinical trials or pharmacokinetic studies are very limited.

There are several distinct areas of concern regarding the association between age and HIV disease.[2] First, older HIV-infected patients may suffer from aging-related comorbid illnesses that can complicate the management of HIV infection, as outlined in detail below. Second, HIV disease may affect the biology of aging, possibly resulting in early manifestations of many clinical syndromes generally associated with advanced age. Third, reduced mucosal and immunologic defenses (such as post-menopausal atrophic vaginitis) and changes in risk behaviors (for example, decrease in condom use because of less concern about pregnancy and increased use of erectile dysfunction drugs) in older adults could lead to increased risk of acquisition and transmission of HIV.[3-4] Finally, because older adults generally are perceived to be at low risk of HIV infection, screening for HIV in this population remains low. For these reasons, HIV infection in many older adults may not be diagnosed until late in the disease process. This section focuses on HIV diagnosis and treatment considerations in the older HIV-infected patient.

HIV Diagnosis and Prevention

Even though many older individuals are engaged in risk behaviors associated with acquisition of HIV, they may be perceived to be at low risk of infection and, as a result, they are less likely to be tested for HIV than younger persons.[5] According to one U.S. survey, 71% of men and 51% of women age 60 years and older continue to be sexually active,[6] with less concern about the possibility of pregnancy contributing to less

condom use. Another national survey reported that among individuals age 50 years or older, condoms were not used during most recent intercourse with 91% of casual partners or 70% of new partners.[7] In addition, results from a CDC survey[8] show that in 2008 only 35% of adults age 45 to 64 years had ever been tested for HIV infection despite the 2006 CDC recommendation that individuals age 13 to 64 years be tested at least once and more often if sexually active.[9] Clinicians must be attuned to the possibility of HIV infection in older patients, including those older than 64 years of age who, based on CDC recommendations, would not be screened for HIV. Furthermore, sexual history taking, risk-reduction counseling, and screening for sexually transmitted diseases (STDs) (if indicated), are important components of general health care for HIV-infected and -uninfected older patients.

Failure to consider a diagnosis of HIV in older persons likely contributes to later disease presentation and initiation of ART.[10] One surveillance report showed that the proportion of patients who progressed to AIDS within 1 year of diagnosis was greater among patients >60 years of age (52%) than among patients younger than 25 years (16%).[1] When individuals >50 years of age present with severe illnesses, AIDS-related opportunistic infections (OIs) need to be considered in the differential diagnosis of the illness.

Initiating Antiretroviral Therapy

Concerns about decreased immune recovery and increased risk of serious non-AIDS events are factors that favor initiating ART in patients >50 years of age regardless of CD4 cell count **(BIII)**. (See Initiating Antiretroviral Therapy in Treatment-Naive Patients.) Data that would favor use of any one of the Panel's recommended initial ART regimens (see What to Start) on the basis of age are not available. The choice of regimen should be informed by a comprehensive review of the patient's other medical conditions and medications. A noteworthy limitation of currently available information is lack of data on the long-term safety of specific antiretroviral (ARV) drugs in older patients, such as use of tenofovir disoproxil fumarate (TDF) in older patients with declining renal function. The recommendations on how frequently to monitor parameters of ART effectiveness and safety for adults age >50 years are similar to those for the general HIV-infected population; however, the recommendations for older adults focus particularly on the adverse events of ART pertaining to renal, liver, cardiovascular, metabolic, and bone health (see Table 13).

HIV, Aging, and Antiretroviral Therapy

The efficacy, pharmacokinetics, adverse effects, and drug interaction potentials of ART in the older adult have not been studied systematically. There is no evidence that the virologic response to ART is different in older patients than in younger patients. However, CD4 T-cell recovery after starting ART generally is less robust in older patients than in younger patients.[11-14] This observation suggests that starting ART at a younger age will result in better immunologic and possibly clinical outcomes.

Hepatic metabolism and renal elimination are the major routes of drug clearance, including the clearance of ARV drugs. Both liver and kidney function may decrease with age, which may result in impaired drug elimination and drug accumulation.[15] Current ARV drug doses are based on pharmacokinetic and pharmacodynamic data derived from studies conducted in subjects with normal organ function. Most clinical trials include only a small proportion of study participants >50 years of age. Whether drug accumulation in the older patient may lead to greater incidence and severity of adverse effects than seen in younger patients is unknown.

HIV-infected patients with aging-associated comorbidities may require additional pharmacologic intervention, making therapeutic management increasingly complex. In addition to taking medications to manage HIV infection and comorbid conditions, many older HIV-infected patients also are taking medications to ameliorate discomfort (e.g., pain medications, sedatives) or to manage adverse effects of

medications (e.g., anti-emetics). They also may self-medicate with over-the-counter medicines or supplements. In the HIV-negative population, polypharmacy is a major cause of iatrogenic problems in geriatric patients.[16] This may be the result of medication errors (by prescribers or patients), nonadherence, additive drug toxicities, and drug-drug interactions. Older HIV-infected patients probably are at an even greater risk of polypharmacy and its attendant adverse consequences than younger HIV-infected or similarly aged HIV-uninfected patients.

Drug-drug interactions are common with ART and easily can be overlooked by prescribers.[17] The available drug interaction information on ARV agents is derived primarily from pharmacokinetic studies performed in a small number of relatively young, HIV-uninfected subjects with normal organ function (see Tables 14-16b). Data from these studies provide clinicians with a basis to assess whether a significant interaction may exist. However, the magnitude of the interaction may be different in older HIV-infected patients than in younger HIV-infected patients.

Nonadherence is the most common cause of treatment failure. Complex dosing requirements, high pill burden, inability to access medications because of cost or availability, limited health literacy including lack of numeracy skills, misunderstanding of instructions, depression, and neurocognitive impairment are among the key reasons for nonadherence.[18] Although many of these factors likely will be more prevalent in an aging HIV-infected population, some data suggest that older HIV-infected patients may be more adherent to ART than younger HIV-infected patients.[19-21] Clinicians should assess adherence regularly to identify any factors, such as neurocognitive deficits, that may make adherence a challenge. One or more interventions such as discontinuation of unnecessary medications; regimen simplification; or use of adherence tools, including pillboxes, daily calendars, and evidence-based behavioral approaches may be necessary to facilitate medication adherence (see Adherence to Antiretroviral Therapy).

Non-AIDS HIV-Related Complications and other Comorbidities

With the reduction in AIDS-related morbidity and mortality observed with effective use of ART, non-AIDS conditions constitute an increasing proportion of serious illnesses in ART-treated HIV-infected populations.[22-24] Heart disease and cancer are the leading causes of death in older Americans.[25] Similarly, for HIV-infected patients on ART, non-AIDS events such as heart disease, liver disease, and cancer have emerged as major causes of morbidity and mortality. Neurocognitive impairment, already a major health problem in aging patients, may be exacerbated by the effect of HIV infection on the brain.[26] That the presence of multiple non-AIDS comorbidities coupled with the immunologic effects of HIV infection could add to the disease burden of an aging HIV-infected person is a concern.[27-29] At present, primary care recommendations are the same for HIV-infected and HIV-uninfected adults and focus on identifying and managing risks of conditions such as heart, liver, and renal disease; cancer; and bone demineralization.[30-32]

Discontinuing Antiretroviral Therapy in Older Patients

Important issues to discuss with aging HIV-infected patients are living wills, advance directives, and long-term care planning including financial concerns. Health care cost sharing (e.g., co-pays, out-of-pocket costs), loss of employment, and other financial-related factors can cause interruptions in treatment. Clinic systems can minimize loss of treatment by helping patients maintain access to insurance.

For the severely debilitated or terminally ill HIV-infected patient, adding palliative care medications, while perhaps beneficial, further increases the complexity and risk of negative drug interactions. For such patients, a balanced consideration of both the expected benefits of ART and the toxicities and negative quality-of-life effects of ART is needed.

Few data exist on the use of ART in severely debilitated patients with chronic, severe, or non-AIDS terminal conditions.[33-34] Withdrawal of ART usually results in rebound viremia and a decline in CD4 cell count. Acute retroviral syndrome after abrupt discontinuation of ART has been reported. In very debilitated patients, if there are no significant adverse reactions to ART, most clinicians would continue therapy. In cases where ART negatively affects quality of life, the decision to continue therapy should be made together with the patient and/or family members after a discussion on the risks and benefits of continuing or withdrawing ART.

Conclusion

HIV infection may increase the risk of many major health conditions experienced by aging adults and possibly accelerate the aging process.[35] As HIV-infected adults age, their health problems become increasingly complex, placing additional demands on the health care system. This adds to the concern that outpatient clinics providing HIV care in the United States share the same financial problems as other chronic disease and primary care clinics and that reimbursement for care is not sufficient to maintain care at a sustainable level.[36] Continued involvement of HIV experts in the care of older HIV-infected patients is warranted. However, given that the current shortage of primary care providers and geriatricians is projected to continue, current HIV providers will need to adapt to the shifting need for expertise in geriatrics through continuing education and ongoing assessment of the evolving health needs of aging HIV-infected patients.[37] The aging of the HIV-infected population also signals a need for more information on long-term safety and efficacy of ARV drugs in older patients.

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